REMARKS

Claims 21, 22, and 25-46 are pending in the present application.

The rejections of Claims 21, 22 and 25 under 35 U.S.C. §102(b) and under 35 U.S.C. §103(a) over Fujikawa et al is respectfully traversed.

In rejecting the claims over Fujikawa et al, the Examiner overlooks the simple fact that, as in the previous rejection over Dahl et al, this reference fails to disclose or suggest isolating, culturing, or manipulating cells derived from synovial (joint) *fluid* as presently claimed and as alleged by the Examiner. It is clear from the disclosure throughout column 1 on page 817 that "synovial tissue" was obtained from seropositive rheumatoid arthritis patients (see page 817, col. 1, first para.) and that the "rheumatoid arthritis synovium" was processed to extract mononuclear cells (see page 817, col. 1, last para.).

As has previously been established, the synovium is the soft tissue which lines the non-cartilaginous surfaces within joints with cavities (synovial joints). This physical structure is distinct from synovial fluid which is a thick, stringy fluid found in the cavities of synovial joints that serves to reduce friction between the articular cartilage and other tissues in joints to lubricate and cushion them during movement. Therefore, Fujikawa et al differs from the claimed invention which relates to a method for culturing cells derived from *joint fluid*, not tissue or lining, to produce osteoclast precursor cells. No disclosure or suggestion is provided in Fujikawa et al to modify their disclosure to recover synovial fluid as opposed to the synovium. As such, Applicants submit that the claimed invention is not anticipated by or obvious in view of Fujikawa et al.

As such, withdrawal of these grounds of rejection is requested.

The rejections of Claims 21, 22 and 25 under 35 U.S.C. §102(b) and under 35 U.S.C. §103(a) over Khalkhali-Ellis et al is obviated by amendment.

In the second column on page 353 Khalkhali-Ellis et al disclose a method in which synovial fluid of juvenile rheumatoid arthritis patients is centrifuged to yield a cell pellet. After discarding the cell-free synovial fluid the cell pellet is reconstituted in RPMI 1640 (referred to as an essential medium on page 9, lines 11-12 of the present specification). This step appears to be analogous to the first step of the previously claimed invention, which states "obtaining cells in a cellular fraction containing granulocytes and lymphocytes from joint fluid by centrifugation" (see also page 9, lines 9-12 of the specification). Following resuspension of the cell pellet in RPMI 1640, the suspension is subjected to Ficoll-Hypaque density centrifugation to separate the granulocytes (i.e., PMNs) from the mononuclear cells (i.e., lymphocytes and monocytes). The MNC fraction was then plated on fetal calf serum coated plastic culture dishes for 24-48 hours (see page 353, col. 2, lines 8-9). Subsequently, the nonadherent cells were removed, pelleted, and plated in RPMI containing10% fetal calf serum, at 37°C in 5% CO2 for at least 2-3 weeks (see page 353, col. 2, lines 9-17).

In the claimed method the "cells" in the "obtaining" and "culturing" steps refers to all the "cells" present in the cell pellet obtained by centrifugation. Flowing from the centrifugation of the presently claimed invention it is clear that the cellular fraction recoved embraces all cells contained therein that carry over from the obtaining step, including granulocytes and lymphocytes. In the method of Claim 21, following centrifugation the recovered cells are directly cultured in an essential medium in the absence of additional cytokines. This is different from the disclosure of Khalkhali-Ellis et al, wherein the cellular fraction recovered after centrifugation is resuspended and a subsequent Ficoll-Hypaque density centrifugation step is conducted to separate granulocytes from the mononuclear cells.

Only the later cells were culutured in Khalkhali-Ellis et al. Thus, Claim 21 cannot be anticipated by Khalkhali-Ellis et al. Further, Khalkhali-Ellis et al fail to disclose or suggest modifying their disclosure to arrive at the claimed invention.

Khalkhali-Ellis et al is similarly deficient with respect to Claim 45. Khalkhali-Ellis et al disclose that the MNC population of the inflammatory cells obtained from synovial fluid of juvenile rheumatoid arthritis patients is made up mainly of T and B lymphocytes, plasma cells, and macrophages. The nonadherent cells that are cultured by Khalkhali-Ellis et al are disclosed as being macrophage depleted (see page 354, col. 2, first para. under "Results"). Therefore, the cell population that is actually cultured by plating in RPMI containing10% fetal calf serum, at 37°C in 5% CO2 for at least 2-3 weeks does not actually contain osteoclast precursor cell. Claim 49 contains the limitations of previously pending Claims 21 and 25 including a recitation of the culturing conditions of a temperature ranging from 35 - 37°C in 5 - 7% CO_2-containing air for 1-3 weeks. Further, and in contrast to the disclosure of Khalkhali-Ellis et al, the cell population that is cultured does contain osteoclast precursor cells and, therefore, Khalkhali-Ellis et al fails to anticipate the claimed invention. Further, Khalkhali-Ellis et al fail to disclose or suggest modifying their disclosure to arrive at the claimed invention.

In view of the foregoing, withdrawal of these grounds of rejection is requested.

Applicants again traverse the Restriction Requirement issued on June 12, 2006. In the outstanding Office Action the Examiner holds that the Examiner maintains that search and examination of Claims 21, 22, and 25 (Group I) and Claims 42-44 (Group II) would impose a serious burden. Applicants respectfully wonder how this could be the case when the Office

has already searched and examined both of these groups together in the same application, which resulted in an Office Action being mailed on November 23, 2005.

The Examiner is reminded that 37 C.F.R. §1.104(b) mandates that an "examiner's action will be complete as to all matters, except that in appropriate circumstances, such as misjoinder of invention, fundamental defects in the application, and the like." Further, MPEP §707.07(g) prohibits piecemeal examination, except for certain special circumstances stating "The examiner ordinarily should reject each claim on all valid grounds available, avoiding, however, undue multiplication of references." From the foregoing, it is clear that if this application was properly examined the Examiner has already fully searched all of Claims 21, 22, and 25 (Group I) and Claims 42-44 (Group II). As such, there can be no burden in further examining both groups in the same invention. For this reason, Applicants request that the Examiner withdraw the Restriction Requirement and examine withdrawn Claims 42-44 in the present application.

Applicants submit that the present application is in condition for allowance. Early notification to this effect is respectfully requested.

Respectfully submitted,

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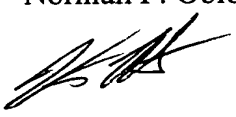

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